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10/568,729	07/13/2006	Neil Cashman	P31382USA	7149

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EXAMINER	
WANG, CHANG YU	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,729	CASHMAN ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27 and 29-51* is/are pending in the application.

4a) Of the above claim(s) *3-8,18,19,23-27,31-38,40,42-46 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,9-17,20-22,29,30,39,41,47-49 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *2/17/06* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/17/06, 8/29/07, 11/11/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Election/Restrictions

1. Applicant's election with traverse of Group I, prion, BSE, peroxynitrite and antibody in the reply filed on August 7, 2006 is acknowledged. The traversal is on the ground(s) that all of the claims share the same special technical feature and the teaching of Kim does not meet the limitations of the claim 1 because Kim does not teach converting inaccessible or blocked target epitopes to accessible target epitopes and does not teach detection agents. Applicant's arguments have been fully considered but they are not found persuasive. In contrast, as previously made of record, Kim does teach the limitation of the claim 1 because Kim teaches a method detecting whether a-synuclein is in a wild-type or non-wild-type confirmation in the presence of Copper and H2O2 (see p. 544, abstract; p.545 materials and methods, Kim et al. (Free Rad. Biol. Med. 2002. 32:544-550), which meets the limitation of the 1st claim. Therefore, claim 1 is anticipated Kim. Therefore, claim 1 does not recite a special technical feature, defined by the PCT rules as a feature that defines a contribution over the prior art. Since the 1st claimed invention has no special technical feature, it cannot share a special technical feature with the other claimed inventions. Thus, Applicant's inventions do not have a single inventive concept and so lack unity of invention. In addition, as previously made of record, Groups I-VII are directed to different technical features that are not required by each other because they have different steps and utilize different products.

The requirement for the rest of restriction is still deemed proper and is therefore made FINAL.

2. Claims 1-27 and 29-51 are pending. Claims 31-38, and 42-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. In addition, claims 3-8, 18, 19, 23-27, 40 and 50 are also withdrawn from further consideration because of non-elected species. Claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 are under examination with respect to prion, BSE, peroxynitrite and antibody in this office action.

Priority

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

4. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see p.6-7). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The elected invention is directed to detecting prion.

Claim Objections

7. Claims 3-8, 18, 19, 23-27, 31-38, 40, 42-46 and 50 are objected to because of the following informalities: the status of the claims 3-8, 18, 19, 23-27, 31-38, 40, 42-46 and 50 are not correct because these claims are withdrawn from consideration. Appropriate correction is required. See MPEP 714 & 37 CFR 1.121.

"In the claim listing, the status of every claim must be indicated after its claim number by using one of the following identifiers in a parenthetical expression: (Original), (Currently amended), (Canceled), (Withdrawn), (Previously presented), (New), and (Not entered)."

Claim 1 is objected to because the recitation "removing unreacted blocking agent" does not contain an article, such as "the". Appropriate correction is required.

Claim 17 is objected to because the claim recites "the antibody comprises 6H4 or 3F4 and the recitation "6H4 or 3F4" is text letters not an antibody molecule. Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 are indefinite because the language recited in independent claims does not make sense. The claims are directed to detecting whether a candidate polypeptide including a target epitope is in a wild-type or non-wild-type confirmation. However, the claim language also encompasses a step to modify a polypeptide. The step of modifying a polypeptide itself would have changed a wild-type polypeptide into a non-wild-type polypeptide and thus would have resulted in a polypeptide in a non-wild-type confirmation. Thus, the claims are indefinite. The rest of the claims are indefinite as depending from indefinite independent claims.

9. Claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: how to convert or modify any inaccessible target to an accessible target and how to detect the change and then determine whether the polypeptide is in a wild-type or non wild-type conformation.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ biological materials, specifically antibody 6H4 or 3F4. Since the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the biological materials are not so obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the biological materials. The specification does not disclose a repeatable process to obtain the biological materials and it is not apparent if the biological materials are readily available to the public. It is noted that Applicant has deposited the biological materials (p. 5 of the specification), but there is no indication in the specification as to public availability. If the deposit is made under the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty and that the biological materials will be irrevocably and without restriction or condition released to the public upon the issuance of a patent,

would satisfy the deposit requirement made herein. If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. §§ 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit will be made (see 37 C.F.R. § 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Applicant's attention is directed to M.P.E.P. §2400 in general, and specifically to §2411.05, as well as to 37 C.F.R. § 1.809(d), wherein it is set forth that "the specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination." The specification should be amended to include this information, however, Applicant is cautioned to avoid the entry of new matter into the specification by adding any other information. Finally,

Applicant is advised that the address for the ATCC has changed, and that the new address should appear in the specification. The new address is:

American Type Culture Collection

10801 University Boulevard

Manassas, VA 20110-2209

11. Claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, were it enabling for detecting more epitopes recognized by antibodies 6H4 and 3F4 in prion protein PrP or a mutant PrP^{Sc} in brain homogenate treated with acid and peroxynitrite in the presence of guanidine than mock treated brain homogenate by immunoprecipitation using antibodies 6H4 and 3F4 would still not reasonably provide enablement for the claimed method of detecting whether a structurally and functionally undefined candidate polypeptide with a unknown target epitope is in a wild-type or non-wild-type conformation by using an unknwon blocking agent to block a unknown accessible epitope in the polypeptide, modifying and determining whether the modified mutant is in a wild-type or non-wild-type conformation as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

"There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is 'undue'. These

factors include, but are not limited to: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)". See MPEP § 2164.01.

Breadth of the claims: Claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 are directed to a method of detecting whether a candidate polypeptide including a target epitope is in a wildtype or non-wildtype conformation comprising contacting the undefined candidate polypeptide with an unknown blocking agent to block accessible epitope, removing the unreated blocking agent, modifying the candidate polypeptide to an unknnown mutant containing an inaccessible target epitope that is converted to accessible epitope, and then determining whether the unknown mutant is in a wildtype or non-wildtype conformation by an unknown detection agent. Independent claims 1, 39 and 49 encompass modifying a genus of unknown target epitopes including accessible and inaccessible target epitopes, and modifying a genus of a structurally and functionally undefined candidate polypeptide, which would have been a mutant, and further to determine whether the undefined mutant is in a wildtype or non-wildtype conformation. Independent claims 1, 39 and 49 also encompass use of a genus of structurally and functionally undefined blocking agents and a genus of structurally and functionally undefined detection agents.

Nature of the invention: The instant invention is based on the finding that brain homogenates treated with acid and/or peroxynitrite in the presence of guanidine reveal more epitopses recognized by antibodies 3F4 and 6H4 as compared to brain homogenates with mock treatment. The instant specification shows that peroxynitrite protects PrP aggregates in brain homogenates from acid modification. The specification also shows that guianidine dissociated PrP aggregates of acid treated brain homogenates. The specification shows that there is an increased PrP immunoprecipitation with 3F4 and 6H4 antibodies in peroxynitrite-treated acid brain homogenates treated guanidine as compared to mock treated brain homogenates.

State of prior art/predictability/experimentation: Based on the specification and prior art, Applicant is enabled for a method of detecting prion protein PrP or PrP^{Sc} in brain homogenate using antibodies 3F4 and 6H4. In addition, Applicant is enabled for a method of detecting more epitopes recognized by antibodies 3F4 and 6H4 in acid and peroxynitrite treated brain homogenate in the presence of guanidine as compared to mock-treated brain homogenate. However, the instant claims are not limited to the methods as set forth above because independent claims 1, 39 and 49 encompass use of structurally and functionally undefined polypeptides, structurally and functionally undefined target epitopes, inaccessible and accessible target epitopes, and also encompass use of structurally and functionally undefined blocking agents and detection agents. The instant specification fails to provide sufficient guidance as to enable a skilled artisan to practice the full scope of the claimed invention because the instant specification fails to teach how to make and use all of the structurally and functionally

undefined targets epitopes, candidate polypeptides, blocking agents and detection agents in the claimed method.

First, the claimed method is directed to a method of determining whether a protein is in a wildtype or non-wildtype confirmation. However, the claimed method itself encompasses a step of modifying polypeptide, which would have changed the wildtype conformation to a non-wildtype conformation since the step of modification recited in the claims is not limited to a specific method. Neither the specification nor the prior art teaches that any modification step can preserve a polypeptide in its wildtype confirmation. It is unpredictable whether all of modification methods would preserve the candidate polypeptide in its wildtype confirmation. The specification fails to teach what specific modification method is and thus a skilled artisan cannot readily make and use the claimed invention without undue experimentation.

Second, the claims fail to limit what the claimed candidate polypeptide is, what the target epitope, accessible and inaccessible epitopes are and what the blocking and detection agents are. The specification only teaches prion PrP treated with acid and peroxynitrite in the presence of guanidine can be detected more epitopes recognized by antibodies 3F4 and 6H4. The claims fail to limit what blocking and detection agents are and thus can be use in the claimed method. The specification fails to teach what other detection agent or method is except immunoprecitation of PrP with antibodies 3F4 and 6H4. The specification fails to teach what other candidate polypeptide, epitopes, blocking agents and detection agents can be used in the claimed method. Thus, it is unpredictable whether all of the structurally and functionally undefined candidate

polypeptides, epitopes, blocking agents and detection agents can be used in the claimed method.

It is known in the art that a single amino acid change could abolish the binding ability of a molecule. For example, a substitution of lysine residue by glutamic acid at position 118 of acidic fibroblast growth factor results in a substantial loss of its biological activity including the binding ability to heparin and its receptor (Burgess et al. J of Cell Bio. 1990, 111:2129-2138). Further, although many amino acid substitutions are possible in any given protein, the position of where such amino acid substitutions can be made is critical for maintaining the function of a protein; i.e. only certain positions can tolerate conservative substitutions without changing the relationship of three dimensional structure and function of the protein (col 2, p. 1306, Bowie et al. Science, 1990, 247:1306-1310). Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would not immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active because conformation is dependent upon surrounding residues; i.e. substitution of non-essential residues can often destroy activity. In addition to a core determinant sequence, the protein-protein interaction also relies on the flanking or noncontiguous residues (see p. 445 the second column, first paragraph, Pawson et al. 2003, Science 300:445-452). The optimal binding motif for a domain is not necessarily suitable for physiological or in vivo interaction. The predictive data always need to be validated by actual analyses in cells (see p. 445, the third column, second paragraph, Pawson et al. 2003, Science 300:445-452).

The instant specification fails to teach what structures/amino acid sequences can or cannot not be included/changed in all candidate polypeptides to preserve an unknown wildtype conformation and unknown target epitope. The instant specification also fails to show what common structures and features are required for the claimed blocking agents and detection agents to be used in the claimed method. The specification fails to teach the structurally and functionally relationship between the prion PrP and other unknown polypeptides. The specification also fails to teach the structurally and functionally relationship between the epitopes recognized by antibodies 3F4 and 6H4 and other unknown epitopes, and nor does the relationship between 3F4/6H4 antibodies and other detection agents. Further, the specification also fails to teach the structurally and functionally relationship between peroxynitrite and other blocking agents or between acid or other modification method or agents.

Therefore, in view of the breadth of the claims, the limited working example, the lack of guidance in the specification, the unpredictability of inventions, and the current status of the prior art, undue experimentation would be required by one of skill in the art to perform in order to practice the claimed invention.

Claim Rejections - 35 USC § 112

12. Claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 are drawn a method of detecting whether a structurally and functionally undefined candidate polypeptide including a unknown target epitope is in a wild-type or non-wild-type conformation comprising contacting the candidate polypeptide with a structurally and functionally undefined blocking agent to block a unknown accessible epitope and modifying the candidate polypeptide to a unknown mutant with an unknown agent to convert an unknown inaccessible to an unknown accessible epitpoe, and then determining whether the unknown mutant is in a wild-type or non-wild-type conformation. The claims encompass a genus of structurally and functionally undefined candidate polypeptide, a genus of structurally and functionally undefined target epitope, accessible target epitope and inaccessible target epitope, a genus of blocking agent and a genus of detection agent. Applicant has not disclosed sufficient species for the broad genera of candidate polypeptide, target epitope, accessible target epitope, inaccessible target epitope, blocking agent and detection agent. The specification only describes detecting more

epitopes recognized by antibodies 3F4 and 6H4 in acid and peroxynitrite treated brain homogenate in the presence of guanidine as compared to mock-treated brain homogenate. However, the claims are not limited to the method as set forth above. The specification fails to provide sufficient species of each genus to demonstrate Applicant's possession of the claimed method.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant is in possession of and what Applicant is claiming. From the specification, it is clear that Applicant is in possession of detecting more epitopes recognized by antibodies 3F4 and 6H4 in acid and peroxynitrite treated brain homogenate in the presence of guanidine as compared to mock-treated brain homogenate. Applicant is not in possession the claimed method of detecting all of the unknown candidate polypeptides with undefined target epitopes (including accessible and inaccessible target epitopes) using undefined blocking agents and detection agents. The specification only describes prion PrP or PrP^{Sc}, epitopes recognized by antibodies 3F4 and 6H4, peroxynitrite as a blocking agent, guanidine to dissociate PrP aggregates and antibodies 3F4 and 6H4 as detection agents. There is no identification of any particular portion of the structure that must be conserved for the claimed genera. The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of candidate polypeptide, the genus of target epitope (including the genus of inaccessible and accessible target epitopes), the genus of blocking agents and the genus of detection agents. There is no

description of the conserved regions which are critical to the function of the claimed genera. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure of the claimed genera to prion PrP or PrP^{Sc}, epitopes recognized by antibodies 3F4 and 6H4, peroxynitrite to block epitopes recognized by antibodies 3F4 and 6H4, guanidine to dissociate PrP aggregates and antibodies 3F4 and 6H4 respectively. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify what other candidate polypeptide, target epitopes, blocking agents, and detection agents might be. Since the common characteristics/features of other candidate polypeptide, target epitopes, blocking agents, and detection agents are unknown, a skilled artisan cannot envison the functional correlations of the genera with the claimed invention. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the genera of candidate polypeptide, target epitopes, blocking agents, and detection agents to be used in the claimed method.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the

encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, the claimed method has not met the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement. See MPEP § 2163.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Applicant is advised that should claim 1 be found allowable, claim 39 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

14. Claims 1, 2, 12, 15-17, 20-22, 29-30, 39, 41, 47-49 and 51 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18-22 of U.S. Patent No. 7041807. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of the claims 18-22 of the ‘807 patent anticipates the instant claims. The claims of the '807 patent is directed to a method for detecting PrP^{Sc} in a biological sample using an antibody that is able to recognize PrP^{Sc} wherein the antibody selectively binds to PrPSc, which is a species anticipate the claimed method that is directed to a method of detecting all forms of polypeptides including PrP^{Sc} using all forms of detecting agents including antibodies against PrP^{Sc}. Thus, the instant application and the ‘807 patent claim a non-distinct invention overlapping in scope.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 are rejected under 35 U.S.C. 102 (b) as being anticipated by US2002/0123072 (Prusiner et al. published Sep 5, 2002). The rejection is based on the subject mater that is enabled within the claims.

Claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 are directed a method of detecting whether a candidate polypeptide including a target epitope is in a wildtype or non-wildtype conformation comprising contacting the undefined candidate polypeptide with an unknown blocking agent to block accessible epitope, removing the unreated blocking agent, modifying the candidate polypeptide to an unknnown mutant containing an inaccessible target epitope that is converted to accessible epitope, and then determining whether the unknown mutant is in a wildtype or non-wildtype conformation by an unknown detection agent. Claim 2 is directed to prion PrP^{Sc}, claim 9 is directed to use of peroxynitrite, claims 15-17 are directed to use of antibodies against prion and claim 41 is directed to use of dissociation enhanced lanthanide fluoroimmunoassay and time-resolved fluorescence.

US2002/0123072 (Prusiner) teaches a method of detecting the presence of a disease related to confirmation of a protein PrP^{Sc} in a sample using an antibody specific for PrP^{Sc} such as 3F4 or antibodies in WO97/10505 (see p. 4, [0042]-p. 5, [0049]; p.6, [0089]-p.7, [0097] ; p. 11-14, examples 1-4; p.15, claims 1-27, in particular), which anticipates the method as recited in instant claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51. Prusiner teaches that samples including brain or other biological samples are pre-treated and treated with acid, chemical or chaotropic salts, denaturing detergents, guanidine hydrochloride or proteinase to denature or unfold proteins as recited in instant claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 (see p. 7, [0098]-p.8, [0103], in particular). Prusiner teaches detection of native PrPc or denatured form of PrPSc with an antibody against PrP using immunoprecipitation or ELISA or time-resolved dissociation-enhanced fluorescence (as in claim 41) (see p. 3, [0022]; p. 8, [0106]-p.9,[0116], in particular). Prusiner teaches pretreatment of samples with antibodies binding to the non-disease conformation of the protein and remove the non-disease protein or pretreatment of samples with acids or alkaline or temperature or chemicals to destroy proteins that are not related to the assayed proteins as in claims 29-30 (see p. 7, [0099], in particular), which meets the limitation as recited in independent claims 1, 39 and 49 and dependent claims 9-14 (including non-elected species in claim 9). Prusiner teaches antibodies to bind to PrP^{Sc} including antibody 3F4 as recited in instant claims 15-17 (see p.9, [0110]-[[0116], in particular). Prusiner teaches detection more PrP^{sc} in denature form of PrP (i.e. non-wildtpe coformation) than in native form with selected antibodies such as 3F4 (see p.9, [0110]-[[0116], in

particular) and also teaches detection of non-wildtype conformation of PrP as an indicator of prion disease as recited in instant claims 20-22 (see p. 8, [0107]-p.9, [0109], in particular). Therefore, Claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 are anticipated by US2002/0123072 (Prusiner).

16. Claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 are rejected under 35 U.S.C. 102 (e) as being anticipated by US6677125 (Prusiner et al. issued Jan 13, 2004, priority Oct 9, 1998).

US6677125 (Prusiner) teaches a method of detecting the presence of a disease related to confirmation of a protein PrP^{Sc} in a sample using an antibody specific for PrP^{Sc} such as 3F4 or antibodies in WO97/10505 (see col.3-6; col.10-12; col.20-24, examples 1-4; cols 25-26, claims 1-9, in particular), which anticipates the method as recited in instant claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51. Prusiner teaches that samples including brain or other biological samples are pre-treated and treated with acid, chemical or chaotropic salts, denaturing detergents, guanidine hydrochloride or proteinase to denature or unfold proteins as recited in instant claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 (see col.12-14, in particular). Prusiner teaches detection of native PrPc or denature form of PrPSc with an antibody against PrP using immunoprecipitation or ELISA or time-resolved dissociation-enhanced fluorescence (as in claim 41) (see p. col. 3-4; col.7-8, in particular). Prusiner teaches pretreatment of samples with an antibodies binding to the non-disease conformation of the protein and removing the non-disease protein or pretreatment of samples with acids or alkaline or

temperature or chemicals to destroy proteins that are not related to the assayed proteins as in claims 29-30 (see col.12-14, in particular), which meets the limitation as recited in independent claims 1, 39 and 49 and dependent claims 9-14 (including non-elected species in claim 9). Prusiner teaches antibodies to bind to PrP^{Sc} including antibody 3F4 as recited in instant claims 15-17 (see col.15-17, in particular). Prusiner teaches detection more PrP^{sc} in denature form of PrP (i.e. non-wildtpe coformation) than in native form with selected antibodies such as 3F4 (see col.17-18, in particular) and also teaches detection of non-wildtype conformation of PrP as an indicator of prion disease as recited in instant claims 20-22 (see col.17-18, in particular). Therefore, Claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 are anticipated by US2002/0123072 (Prusiner).

17. Claims 1-2, 9-17, 20-22, 29-30, 39, 41, 47-49 and 51 are rejected under 35 U.S.C. 102(e) as being anticipated by US7041807 (Cashman et al., issued May 9, 2006, priority Jun 23, 1999). The rejection is as set forth above in section of double patenting.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention “by another,” or by an appropriate showing under 37 CFR 1.131.

US7041807 teaches a method for detecting PrP^{Sc} in a biological sample using an antibody that is able to recognize PrP^{Sc} wherein the antibody selectively binds to PrPSc, which is a species anticipate the claimed method that is directed to a method of detecting all forms of polypeptides including PrP^{Sc} using all forms of detecting agents including antibodies against PrP^{Sc} (see col. 11-14; col. 18-19; col. 25-28, in particular).

Conclusion

18. NO CLAIM IS ALLOWED.

19. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
November 25, 2008

/Jeffrey Stucker/
Supervisory Patent Examiner, Art Unit 1649